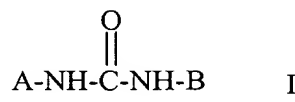


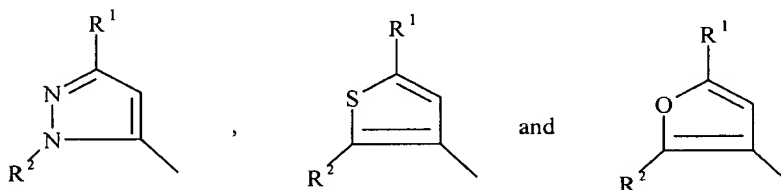
The listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently Amended) A method for the treatment of a disease other than cancer mediated by p38 which comprises administering a compound of formula I or a pharmaceutically acceptable salt thereof



wherein A is a heteroaryl selected from the group consisting of



wherein  $R^1$  is selected from the group consisting of  $C_3$ - $C_{10}$  alkyl,  $C_3$ - $C_{10}$  cycloalkyl, up to per-halosubstituted  $C_1$ - $C_{10}$  alkyl and up to per-halosubstituted  $C_3$ - $C_{10}$  cycloalkyl;

B is a substituted or unsubstituted, up to tricyclic, aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 5- or 6-member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur, wherein if B is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and  $X_n$ ,

wherein n is 0-3 and each X is independently selected from the group consisting of  $-CN$ ,  $CO_2R^5$ ,  $-C(O)NR^5R^{5'}$ ,  $-C(O)R^5$ ,  $-NO_2$ ,  $-OR^5$ ,  $-SR^5$ ,  $-NR^5R^{5'}$ ,

-NR<sup>5</sup>C(O)OR<sup>5'</sup>, -NR<sup>5</sup>C(O)R<sup>5'</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2-10</sub>-alkenyl, C<sub>1-10</sub>-alkoxy, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>7</sub>-C<sub>24</sub> alkaryl, C<sub>3</sub>-C<sub>13</sub> heteroaryl, C<sub>4</sub>-C<sub>23</sub> alkheteroaryl, substituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted C<sub>2-10</sub>-alkenyl, substituted C<sub>1-10</sub>-alkoxy, substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl, substituted C<sub>4</sub>-C<sub>23</sub> alkheteroaryl and -Y-Ar;

where X is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>5</sup>, -C(O)R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5'</sup>, -OR<sup>5</sup>, -SR<sup>5</sup>, -NR<sup>5</sup>R<sup>5'</sup>, -NO<sub>2</sub>, -NR<sup>5</sup>C(O)R<sup>5'</sup>, -NR<sup>5</sup>C(O)OR<sup>5'</sup> and halogen up to per-halosubstitution;

wherein R<sup>5</sup> and R<sup>5'</sup> are independently selected from H, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2-10</sub>-alkenyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>13</sub> heteroaryl, C<sub>7</sub>-C<sub>24</sub> alkaryl, C<sub>4</sub>-C<sub>23</sub> alkheteroaryl, up to per-halosubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, up to per-halosubstituted C<sub>2-10</sub>-alkenyl, up to per-halosubstituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl, up to per-halosubstituted C<sub>6</sub>-C<sub>14</sub> aryl and up to per-halosubstituted C<sub>3</sub>-C<sub>13</sub> heteroaryl,

wherein Y is - O-, -S-, -N(R<sup>5</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -NR<sup>5</sup>C(O)NR<sup>5</sup>R<sup>5'</sup>-, -NR<sup>5</sup>C(O)-, -C(O)NR<sup>5</sup>-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>5</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-, -CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>5</sup>)(CH<sub>2</sub>)<sub>m</sub>-,

m = 1-3, and X<sup>a</sup> is halogen; and

Ar is a 5-10 member aromatic structure containing 0-2 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up to per-halosubstitution and optionally substituted by Z<sub>n1</sub>, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5'</sup>, -C(O)NR<sup>5</sup>, -NO<sub>2</sub>, -OR<sup>5</sup>, -SR<sup>5</sup>, -NR<sup>5</sup>R<sup>5'</sup>, -NR<sup>5</sup>C(O)OR<sup>5'</sup>, -OC(O)R<sup>5</sup>, -NR<sup>5</sup>C(O)R<sup>5'</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>13</sub> heteroaryl, C<sub>7</sub>-C<sub>24</sub> alkaryl, C<sub>4</sub>-C<sub>23</sub> alkheteroaryl, substituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl, substituted C<sub>7</sub>-C<sub>24</sub> alkaryl and substituted C<sub>4</sub>-C<sub>23</sub> alkheteroaryl;

wherein if Z is a substituted group, it is substituted by the one or more substituents independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5'</sup>, -OR<sup>5</sup>, -SR<sup>5</sup>, -NO<sub>2</sub>, -NR<sup>5</sup>R<sup>5'</sup>, -NR<sup>5</sup>C(O)R<sup>5'</sup> and -NR<sup>5</sup>C(O)OR<sup>5'</sup>, and

wherein R<sup>2</sup> is C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, substituted C<sub>6</sub>-C<sub>14</sub> aryl or substituted C<sub>3</sub>-C<sub>14</sub> heteroaryl,

wherein if R<sup>2</sup> is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and V<sub>n</sub>,

wherein  $n = 0-3$  and each  $V$  is independently selected from the group consisting of -CN,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{OC}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ ,  $-\text{SO}_2\text{R}^5$ ,  $-\text{SOR}^5$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$ ,  $-\text{NO}_2$ ,  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{C}_3\text{-C}_{10}$  cycloalkyl,  $\text{C}_6\text{-C}_{14}$  aryl,  $\text{C}_3\text{-C}_{13}$  heteroaryl,  $\text{C}_7\text{-C}_{24}$  alkaryl,  $\text{C}_4\text{-C}_{24}$  alkheteroaryl, substituted  $\text{C}_1\text{-C}_{10}$  alkyl, substituted  $\text{C}_3\text{-C}_{10}$  cycloalkyl, substituted  $\text{C}_6\text{-C}_{14}$  aryl, substituted  $\text{C}_3\text{-C}_{13}$  heteroaryl, substituted  $\text{C}_7\text{-C}_{24}$  alkaryl and substituted  $\text{C}_4\text{-C}_{24}$  alkheteroaryl,

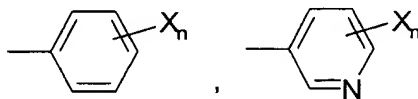
where  $V$  is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, -CN,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$  and  $-\text{NO}_2$ ,

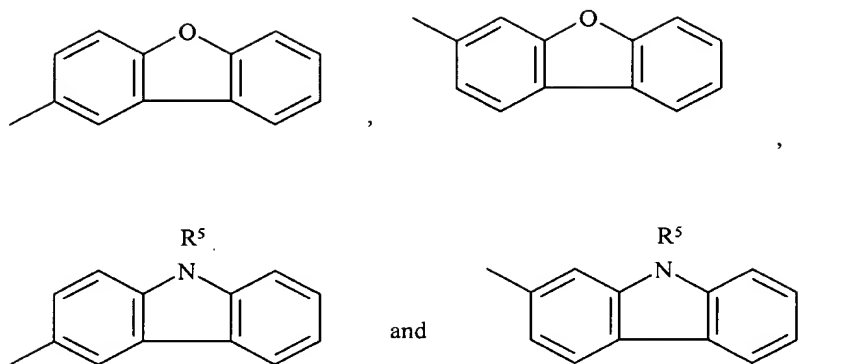
wherein  $\text{R}^5$  and  $\text{R}^{5'}$  are each independently as defined above.

2. (Original) A method as in claim 1, wherein  $\text{R}^2$  is selected from substituted or unsubstituted members of the group consisting of phenyl and pyridinyl, and the substituents for  $\text{R}^2$  are selected from the group consisting of halogen, up to per-halosubstitution and  $\text{Y}_n$ , wherein  $n = 0-3$ , and each  $\text{Y}$  is independently selected from the group consisting of substituted and unsubstituted  $\text{C}_1\text{-C}_6$  alkyl,  $\text{C}_3\text{-C}_{10}$  cycloalkyl,  $\text{C}_6\text{-C}_{10}$  aryl,  $-\text{NO}_2$ ,  $-\text{NH}_2$ ,  $-\text{C}(\text{O})\text{-C}_{1-6}$  alkyl,  $-\text{C}(\text{O})\text{N-(C}_{1-6}\text{ alkyl)}_2$ ,  $-\text{C}(\text{O})\text{NH-C}_{1-6}$  alkyl,  $-\text{O-C}_{1-6}$  alkyl,  $-\text{NHC}(\text{O})\text{H}$ ,  $-\text{NHC}(\text{O})\text{OH}$ ,  $-\text{N(C}_{1-6}\text{ alkyl)C}(\text{O})\text{-C}_{1-6}$  alkyl,  $-\text{N-(C}_{1-6}\text{ alkyl)C}(\text{O})\text{-C}_{1-6}$  alkyl,  $-\text{NHC}(\text{O})\text{-C}_{1-6}$  alkyl,  $-\text{OC}(\text{O})\text{NH C}_{6-14}$  aryl,  $-\text{NHC}(\text{O})\text{O-C}_{1-6}$  alkyl,  $-\text{S}(\text{O})\text{-C}_{1-6}$  alkyl and  $-\text{SO}_2\text{-C}_{1-6}$  alkyl,

wherein if  $\text{Y}$  is a substituted group, it is substituted by one or more halogen, up to per-halosubstitution.

3. (Original) A method as in claim 1, wherein  $\text{B}$  is up to a tricyclic aromatic ring structure selected from the group consisting of





which is substituted or unsubstituted by halogen, up to per-halosubstitution, and wherein

$n = 0-3$  and

each X is independently selected from the group consisting of  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{NO}_2$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$ ,  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{C}_2\text{-C}_{10}$ -alkenyl,  $\text{C}_1\text{-C}_{10}$ -alkoxy,  $\text{C}_3\text{-C}_{10}$  cycloalkyl,  $\text{C}_6\text{-C}_{14}$  aryl,  $\text{C}_7\text{-C}_{24}$  alkaryl,  $\text{C}_3\text{-C}_{13}$  heteroaryl,  $\text{C}_4\text{-C}_{23}$  alkheteroaryl, and substituted  $\text{C}_1\text{-C}_{10}$  alkyl, substituted  $\text{C}_2\text{-C}_{10}$ -alkenyl, substituted  $\text{C}_1\text{-C}_{10}$ -alkoxy, substituted  $\text{C}_3\text{-C}_{10}$  cycloalkyl, substituted  $\text{C}_4\text{-C}_{23}$  alkheteroaryl and  $-\text{Y-Ar}$ ;

wherein if X is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{NO}_2$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$  and halogen up to per-halosubstitution;

wherein  $\text{R}^5$  and  $\text{R}^{5'}$  are independently selected from H,  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{C}_2\text{-C}_{10}$ -alkenyl,  $\text{C}_3\text{-C}_{10}$  cycloalkyl,  $\text{C}_6\text{-C}_{14}$  aryl,  $\text{C}_3\text{-C}_{13}$  heteroaryl,  $\text{C}_7\text{-C}_{24}$  alkaryl,  $\text{C}_4\text{-C}_{23}$  alkheteroaryl, up to per-halosubstituted  $\text{C}_1\text{-C}_{10}$  alkyl, up to per-halosubstituted  $\text{C}_2\text{-C}_{10}$ -alkenyl, up to per-halosubstituted  $\text{C}_3\text{-C}_{10}$  cycloalkyl, up to per-halosubstituted  $\text{C}_6\text{-C}_{14}$  aryl and up to per-halosubstituted  $\text{C}_3\text{-C}_{13}$  heteroaryl,

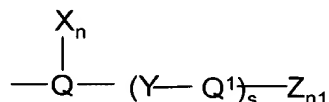
wherein Y is  $-\text{O}-$ ,  $-\text{S}-$ ,  $-\text{N}(\text{R}^5)-$ ,  $-(\text{CH}_2)_m-$ ,  $-\text{C}(\text{O})-$ ,  $-\text{CH}(\text{OH})-$ ,  $-(\text{CH}_2)_m\text{O}-$ ,  $-\text{NR}^5\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})-$ ,  $-\text{C}(\text{O})\text{NR}^5-$ ,  $-(\text{CH}_2)_m\text{S}-$ ,  $-(\text{CH}_2)_m\text{N}(\text{R}^5)-$ ,  $-\text{O}(\text{CH}_2)_m-$ ,  $-\text{CHX}^a-$ ,  $-\text{CX}^a_2-$ ,  $-\text{S}-(\text{CH}_2)_m-$  and  $-\text{N}(\text{R}^5)(\text{CH}_2)_m-$ ,

$m = 1-3$ , and  $\text{X}^a$  is halogen; and

Ar is a 5- or 6-member aromatic structure containing 0-2 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up to per-halosubstitution and optionally substituted by  $\text{Z}_{n1}$ , wherein  $n1$  is 0 to 3 and each Z is independently selected from the group consisting of  $-\text{CN}$ ,  $-\text{C}(\text{O})\text{R}^5$ ,

-CO<sub>2</sub>R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5'</sup>, -C(O)R<sup>5</sup>, -NO<sub>2</sub>, -OR<sup>5</sup>, -SR<sup>5</sup>, -NR<sup>5</sup>R<sup>5'</sup>, -NR<sup>5</sup>C(O)OR<sup>5'</sup>,  
 -NR<sup>5</sup>C(O)R<sup>5'</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>13</sub> heteroaryl, C<sub>7</sub>-C<sub>24</sub> alkaryl,  
 C<sub>4</sub>-C<sub>23</sub> alkheteroaryl, substituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl, substituted C<sub>7</sub>-  
 C<sub>24</sub> alkaryl and substituted C<sub>4</sub>-C<sub>23</sub> alkheteroaryl; wherein if Z is a substituted group, it is  
 substituted by one or more substituents independently selected from the group consisting of -  
 CN, -CO<sub>2</sub>R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5'</sup>, -OR<sup>5</sup>, -SR<sup>5</sup>, -NO<sub>2</sub>, -NR<sup>5</sup>R<sup>5'</sup>, -NR<sup>5</sup>C(O)R<sup>5'</sup> and -NR<sup>5</sup>C(O)OR<sup>5'</sup>.

4. (Previously Presented) A method of claim 1, wherein B is



wherein

Y is selected from the group consisting of -O-, -S-, -CH<sub>2</sub>-, -SCH<sub>2</sub>-, -CH<sub>2</sub>S-,  
 -CH(OH)-, -C(O)-, -CX<sup>a</sup><sub>2</sub>, -CX<sup>a</sup>H-, -CH<sub>2</sub>O- and -OCH<sub>2</sub>-,

X<sup>a</sup> is halogen,

Q is a six member aromatic structure containing 0-2 nitrogen, substituted or  
 unsubstituted by halogen, up to per-halosubstitution;

Q<sup>1</sup> is a mono- or bicyclic aromatic structure of 3 to 10 carbon atoms and 0-4 members  
 of the group consisting of N, O and S, substituted or unsubstituted by halogen up to per-  
 halosubstitution,

s = 0 or 1, and

X, Z, n and n1 are as defined in claim 1.

5. (Original) A method as in claim 4, wherein

Q is phenyl or pyridinyl, substituted or unsubstituted by halogen, up to per-  
 halosubstitution,

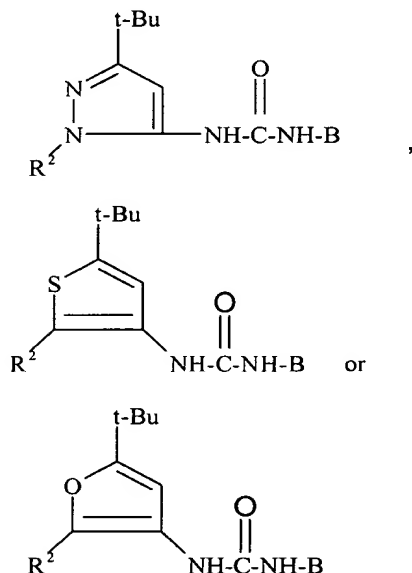
Q<sup>1</sup> is selected from the group consisting of phenyl, pyridinyl, naphthyl, pyrimidinyl,  
 quinoline, isoquinoline, imidazole and benzothiazolyl, substituted or unsubstituted by  
 halogen, up to per-halo substitution, or Y-Q<sup>1</sup> is phthalimidinyl substituted or unsubstituted by  
 halogen up to per-halo substitution, and

Z and X are independently selected from the group consisting of -R<sup>6</sup>, -OR<sup>6</sup> and -  
 NHR<sup>7</sup>, wherein R<sup>6</sup> is hydrogen, C<sub>1</sub>-C<sub>10</sub>-alkyl or C<sub>3</sub>-C<sub>10</sub>-cycloalkyl and R<sup>7</sup> is selected from the

group consisting of hydrogen, C<sub>3</sub>-C<sub>10</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub>-cycloalkyl and C<sub>6</sub>-C<sub>10</sub>-aryl, wherein R<sup>6</sup> and R<sup>7</sup> can be substituted by halogen or up to per-halosubstitution.

6. (Original) A method as in claim 4, wherein Q is phenyl, Q<sup>1</sup> is phenyl or pyridinyl, Y is -O-, -S- or -CH<sub>2</sub>-, and X and Z are independently Cl, F, CF<sub>3</sub>, NO<sub>2</sub> or CN.

7. (Original) A method as in claim 1, which comprises administering a compound of one of the formulae or a pharmaceutically acceptable salt thereof:



wherein B and R<sup>2</sup> are as defined in claim 1.

8. (Original) A method as in claim 7, wherein R<sup>2</sup> is selected from substituted and unsubstituted members of the group consisting of phenyl and pyridinyl, wherein if R<sup>2</sup> is a substituted group, it is substituted by one or more substituents selected from the group consisting of halogen and W<sub>n</sub>, wherein n = 0-3, and W is selected from the group consisting of -NO<sub>2</sub>, -C<sub>1-3</sub> alkyl, -NH(O)CH<sub>3</sub>, -CF<sub>3</sub>, -OCH<sub>3</sub>, -F, -Cl, -NH<sub>2</sub>, -OC(O)NH up to per-halosubstituted phenyl, -SO<sub>2</sub>CH<sub>3</sub>, pyridinyl, phenyl, up to per-halosubstituted phenyl and C<sub>1</sub>-C<sub>6</sub> alkyl substituted phenyl.

9. (Original) A method as in claim 1, comprising administering an amount of compound of formula I effective to inhibit p38.

10. (Original) A method as in claim 1, wherein the compound of formula I displays p38 activity ( $IC_{50}$ ) better than  $10\mu M$  as determined by an in-vitro kinase assay.

11. (Original) A method according to claim 1, wherein the disease is mediated by a cytokine or protease regulated by p38.

12. (Previously Presented) A method according to claim 1, wherein  $R^1$  is t-butyl.

13. (Previously Presented) A method according to claim 12, comprising administering an amount of a compound of formula I effective to inhibit p38.

14. (Original) A method according to claim 1, comprising administering an amount of a compound of formula I effective to inhibit production of a disease-mediating cytokine or protease.

15. (Original) A method according to claim 1, wherein the disease is an inflammatory or immunomodulatory disease.

16. (Original) A method according to claim 1, wherein the disease is rheumatoid arthritis, osteoarthritis, osteoporosis, asthma, septic shock, inflammatory bowel disease, or the result of host-versus-graft reactions.

17. (Previously Presented) A method for the treatment of a disease other than cancer mediated by p38 which comprises administering a compound of formula I or a pharmaceutically acceptable salt thereof



wherein B is phenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl,

benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl substituted by -Y-Ar; and is optionally substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and  $X_n$ ,

wherein n is 0-3 and each X is independently selected from the group consisting of -CN,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{NO}_2$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$ ,  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{C}_2\text{-C}_{10}$  alkenyl,  $\text{C}_1\text{-C}_{10}$  alkoxy,  $\text{C}_3\text{-C}_{10}$  cycloalkyl, phenyl, pyridinyl, naphthyl, isoquinolinyl, quinolinyl up to per halo-substituted  $\text{C}_1\text{-C}_{10}$  alkyl, up to per halo-substituted  $\text{C}_2\text{-C}_{10}$  alkenyl, up to per halo-substituted  $\text{C}_1\text{-C}_{10}$  alkoxy, up to per halo-substituted  $\text{C}_3\text{-C}_{10}$  cycloalkyl, and

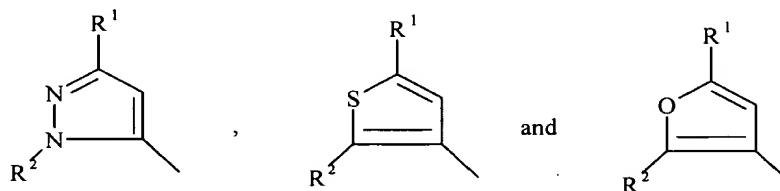
wherein  $\text{R}^5$  and  $\text{R}^{5'}$  are independently selected from H,  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{C}_2\text{-C}_{10}$  alkenyl,  $\text{C}_3\text{-C}_{10}$  cycloalkyl, up to per-halosubstituted  $\text{C}_1\text{-C}_{10}$  alkyl, up to per-halosubstituted  $\text{C}_2\text{-C}_{10}$  alkenyl and up to per-halosubstituted  $\text{C}_3\text{-C}_{10}$  cycloalkyl,

wherein Y is -O-, -S-,  $-\text{N}(\text{R}^5)\text{-}$ ,  $-(\text{CH}_2)_m\text{-}$ ,  $-\text{C}(\text{O})\text{-}$ ,  $-\text{CH}(\text{OH})\text{-}$ ,  $-(\text{CH}_2)_m\text{O-}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{NR}^5\text{NR}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{-}$ ,  $-\text{C}(\text{O})\text{NR}^5\text{-}$ ,  $-(\text{CH}_2)_m\text{S-}$ ,  $-(\text{CH}_2)_m\text{N}(\text{R}^5)\text{-}$ ,  $-\text{O}(\text{CH}_2)_m\text{-}$ ,  $-\text{CHX}^a$ ,  $-\text{CX}^a_2\text{-}$ ,  $-\text{S}(\text{CH}_2)_m\text{-}$  and  $-\text{N}(\text{R}^5)(\text{CH}_2)_m\text{-}$ ,

$m = 1\text{-}3$ , and  $\text{X}^a$  is halogen; and

Ar is phenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzofuryl, benzothienyl, indolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl or benzisothiazolyl, optionally substituted by halogen up to per-halosubstitution and optionally substituted by  $\text{Z}_{n1}$ , wherein  $n1$  is 0 to 3 and each Z is independently selected from the group consisting of  $-\text{CN}$ ,  $=\text{O}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{C}(\text{O})\text{-NR}^5$ ,  $-\text{NO}_2$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$ ,  $-\text{SO}_2\text{R}^5$ ,  $\text{SO}_2\text{NR}^5\text{R}^{5'}$ ,  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{C}_1\text{-C}_{10}$  alkoxy,  $\text{C}_3\text{-C}_{10}$  cycloalkyl, up to per halo-substituted  $\text{C}_1\text{-C}_{10}$  alkyl, and up to per halo-substituted  $\text{C}_3\text{-C}_{10}$  cycloalkyl, and

wherein A is a heteroaryl selected from the group consisting of





wherein R<sup>1</sup> is selected from the group consisting of C<sub>3</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, up to per-halosubstituted C<sub>1</sub>-C<sub>10</sub> alkyl and up to per-halosubstituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl,

wherein R<sup>2</sup> is C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, substituted C<sub>6</sub>-C<sub>14</sub> aryl or substituted C<sub>3</sub>-C<sub>14</sub> heteroaryl,

wherein if R<sup>2</sup> is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and V<sub>n</sub>,

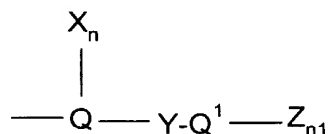
wherein n = 0-3 and each V is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5'</sup>, -OR<sup>5</sup>, -SR<sup>5</sup>, -NR<sup>5</sup>R<sup>5'</sup>, -C(O)R<sup>5</sup>, -OC(O)NR<sup>5</sup>R<sup>5'</sup>, -NR<sup>5</sup>C(O)OR<sup>5'</sup>, -SO<sub>2</sub>R<sup>5</sup>, -SOR<sup>5</sup>, -NR<sup>5</sup>C(O)R<sup>5'</sup>, -NO<sub>2</sub>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>13</sub> heteroaryl, C<sub>7</sub>-C<sub>24</sub> alkaryl, C<sub>4</sub>-C<sub>24</sub> alkheteroaryl, substituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl, substituted C<sub>6</sub>-C<sub>14</sub> aryl, substituted C<sub>3</sub>-C<sub>13</sub> heteroaryl, substituted C<sub>7</sub>-C<sub>24</sub> alkaryl and substituted C<sub>4</sub>-C<sub>24</sub> alkheteroaryl,

where V is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, -CN, -CO<sub>2</sub>R<sup>5</sup>, -C(O)R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5'</sup>, -NR<sup>5</sup>R<sup>5'</sup>, -OR<sup>5</sup>, -SR<sup>5</sup>, -NR<sup>5</sup>C(O)R<sup>5'</sup>, -NR<sup>5</sup>C(O)OR<sup>5'</sup> and -NO<sub>2</sub>,

wherein R<sup>5</sup> and R<sup>6</sup> are each independently as defined above.

18. (Previously Presented) A method as in claim 17 wherein R<sup>2</sup> is phenyl, substituted phenyl, pyridinyl or substituted pyridinyl.

19. (Previously Presented) A method of claim 17, wherein B is



wherein

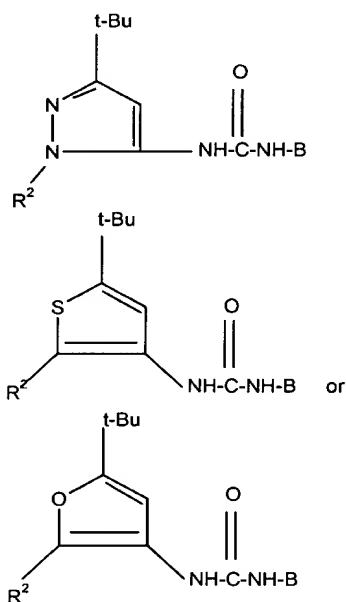
Y is as defined in claim 17,

Q and Q<sup>1</sup> are independently selected from the group consisting of phenyl, pyridinyl, naphthyl, pyrimidinyl, quinoline, isoquinoline, imidazole and benzothiazolyl, optionally substituted by halogen, up to per-halo substitution, and

Z and X are independently selected from the group consisting of  $-R^6$ ,  $-OR^6$  and  $-NHR^7$ , wherein  $R^6$  is hydrogen,  $C_1$ - $C_{10}$ -alkyl or  $C_3$ - $C_{10}$ -cycloalkyl and  $R^7$  is selected from the group consisting of hydrogen,  $C_3$ - $C_{10}$ -alkyl, and  $C_3$ - $C_6$ -cycloalkyl wherein  $R^6$  and  $R^7$  can be substituted by halogen or up to per-halosubstitution.

20. (Previously Presented) A method as in claim 19, wherein Q is phenyl,  $Q^1$  is phenyl or pyridinyl, Y is  $-O-$ ,  $-S-$  or  $-CH_2$ , and X and Z are independently Cl, F,  $CF_3$ ,  $NO_2$  or CN.

21. (Previously Presented) A method as in claim 17, which comprises administering a compound of one of the formulae or a pharmaceutically acceptable salt thereof:



wherein B and  $R^2$  are as defined in claim 17.

22. (Previously Presented) A method as in claim 21, wherein  $R^2$  is phenyl, pyridinyl, substituted phenyl or substituted pyridinyl.

23. (Previously Presented) A method as in claim 17, comprising administering an amount of compound of formula I effective to inhibit p38.

24. (Previously Presented) A method as in claim 17, wherein the compound of formula I displays p38 activity ( $IC_{50}$ ) better than  $10\mu M$  as determined by an in-vitro kinase assay.

25. (Previously Presented) A method according to claim 17, wherein the disease is mediated by a cytokine or protease regulated by p38.

26. (Previously Presented) A method according to claim 17, wherein  $R^1$  is t-butyl.

27. (Previously Presented) A method according to claim 26, comprising administering an amount of a compound of formula I effective to inhibit p38.

28. (Previously Presented) A method according to claim 17, comprising administering an amount of a compound of formula I effective to inhibit production of a disease-mediating cytokine or protease.

29. (Previously Presented) A method according to claim 17, wherein the disease is an inflammatory or immunomodulatory disease.

30. (Previously Presented) A method according to claim 17, wherein the disease is rheumatoid arthritis, osteoarthritis, osteoporosis, asthma, septic shock, inflammatory bowel disease, or the result of host-versus-graft reactions.

31. (New) A method as in claim 1, wherein  $R^2$  is phenyl.

32. (New) A method as in claim 1, wherein  $R^2$  is a substituted  $C_6-C_{14}$  aryl or substituted  $C_3-C_{14}$  heteroaryl.